REMARKS

Claims 9-12 are pending. Claims 1-8 are cancelled by a preliminary amendment filed March 23, 2004, without prejudice to the prosecution of their subject matter in other applications. Claims 9, 11 and 12 are currently amended. Since support for the amendments can be found throughout the specification and claims as originally filed, there is no new matter added as a consequence of the amendments to the claims.

Applicants are required to comply with the sequence rules under 37 C.F.R. §§ 1.821-1.825 by inserting sequence identifiers for all recited sequences. The Information Disclosure Statement filed March 5, 2002 is currently under consideration. Applicants have submitted herewith a second substitute sequence listing and corresponding amendments to the specification to comply with sequence disclosure rules under 37 C.F.R. §§ 1.821-1.825 .

Claims 9-12 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter of the claimed invention. Claims 9-12 are rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. Claims 9-12 are rejected under 35 U.S.C. § 103(a), as being allegedly unpatentable over Kutchera *et al.* (Proc. Natl Acad Sci. USA 1996, 93(10): 4816-4820, henceforth referred to as Kutchera) and Dannenberg et al., (U.S. Patent No. 6,200,760, henceforth referred to as Dannenberg). For reasons set forth below, it is respectfully requested that the rejections be withdrawn and that the claims be deemed allowable.

Sequence Listing Compliance

In the Official Action, the Examiner required Applicants to insert Sequence Identifiers to comply with the Sequence Listing Rules. In preparing our response, it was noted that an additional sequence had been disclosed in Figure 2, but not included in previous versions of the Sequence Listing. Accordingly, Applicants herewith submit a Second Substitute Sequence Listing in paper and computer readable form (on floppy disk). The Substitute Sequence Listing includes the additional sequence disclosed in Fig. 2 but not previously submitted. The sequence listing has therefore been amended so that a new SEQ ID NO:6 is introduced which corresponds to previously disclosed SEQ ID NO:5. Currently listed SEQ ID NO:5 is the previously unlisted sequence from Fig. 2. Thus the substitute sequence listing submitted in accordance with 37 C.F.R. §1.821(g) is fully supported by the specification as filed. I hereby state that the content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e), are the same and contain no new matter.

The Claims Are Definite

Claims 9-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the phrase "measuring the reporter gene activity" in Claim 9 allegedly renders the claim indefinite. It is unclear, according to the Examiner, whether the reporter gene activity is directly measured or if the activity of the reporter gene encoded protein is being measured. Applicants note that in the method of utilizing reporter gene constructs, the assumption that expression of the reporter gene essentially reflects activity of the reporter gene itself is well known and commonly accepted in the relevant art. However, in the interest of expediting allowance of the instant application, Applicants have amended claim 9 to replace "measuring reporter gene activity" with "measuring the expression of the encoded reporter protein". Applicants assert that "expression" rather than "activity" is more appropriate, in that the detectable expression of the reporter gene is what is measured, by detecting either enzymatic function or some other property (e.g. fluorescence or immune reactivity) of the reporter product. Although fluorescence could be considered "activity", Applicants consider reference to "expression" rather than "activity" more precise as the reporter gene product may conceivably play a passive role.

The Examiner has further alleged that it will not be clear to a skilled practitioner whether a compound identified by the method of claim 9 is indeed a transcriptional inhibitor of the Cox-2 promoter. Applicants are said to have omitted control steps which may determine if the activity seen is primarily due to a direct

interaction between inducer and test compound rather than test compound and the promoter. Therefore the method is alleged to lack essential step(s).

Applicants respectfully disagree with the Examiner's grounds for rejection. The ability of the test inhibitor to interact with a Cox-2 stimulating agent has value in identifying agents that inhibit transcription of Cox-2, as the stimulating agent may be the same or functionally equivalent to stimulating agents that operate *in vivo*. However, even if this were not the case, the possibility that in certain instances the test inhibitor were to interact with the stimulator would not negate patentability, as not all embodiments of a claim need be operable. Moreover, claim 9 is amended so that the requirement for a stimulator is removed provided that the method is conducted under conditions that allow the transcription of the cyclooxygenase 2 promoter to be active. With the amended language, the method may be practiced in either the presence or the absence of a stimulator.

The Examiner has rejected claim 11 as being indefinite for allegedly failing to clarify which human promoter is being referred to. Applicants have amended claim 11 to read "the cyclooxygenase 2 promoter is isolated from human" as suggested by the Examiner to overcome this rejection.

Similarly claim 12 is rejected as allegedly unclear in reciting "PMA". In response, claim 12 has been amended to recite "phorbol myristate acetate" in place of the alleged unclear term "PMA".

For the reasons set forth above, Applicants respectfully suggest that Claims 9-12 are definite so the rejections under 35 U.S.C. § 112, second paragraph, should be withdrawn.

The Claims Are Enabled

Claims 9-12 is rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for a method of identification of compounds that inhibit transcription of the COX-2 gene promoter since a skilled practitioner will not be able to conclude whether the identified compound inhibits the inducer directly rather than the promoter itself.

As set forth above, the Examiner has identified a particular *hypothetical* embodiment of the claim, wherein the test inhibitor would interact with the stimulator rather than the Cox-2 promoter- as the basis for the rejection. Applicants assert that the rejection is not sound, as even if these special circumstances were to apply, the result would confer predictive value. In addition, Applicants maintain that the skilled artisan would, using standard techniques, readily be able to determine whether or not the stimulator is indeed the target for the test inhibitor by merely using an unrelated alternate stimulator: if the test inhibitor targetted the inhibitor, it would be expected to have negligible effect on reporter expression in the context of the alternate stimulator.

For the reasons set forth above, Applicants respectfully suggest that Claims 9-12 are fully enabled so the rejections under 35 U.S.C. § 112, first paragraph, should be withdrawn.

The Claims Are Not Obvious

Claims 9-12 are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Kutchera and Dannenberg. The Examiner alleges that Kutchera teaches a 1.9 kb human Cox-2 promoter linked to a luciferase gene but concedes (at page 8, second paragraph of the Office Action mailed January 26, 2005) that use for screening of compounds is not disclosed by this reference. Dannenberg teaches a method for screening for compounds using the human Cox-2 promoter in the presence of PMA and ion. The Examiner concedes that Dannenberg describes use of a smaller 1.4 kb human Cox-2 promoter instead of the 1.9 kb promoter used in the present invention. The Examiner alleges that it would have been obvious to a person of ordinary skill to combine the teachings of Kutchera and Dannenberg and perform tests to identify a test compound using a 1.9 kb Cox-2 promoter.

Applicants note that there are important distinguishing features between the present invention and cited references. First, the cell systems used in Kutchera (HCT-116, DLD-1, Caco-2, LS 174T and SK-CO-1) and Dannenberg (1483 squamous carcinomas and SW1353 chondrocyte line) are distinct from Jurkat cells (a human T-cell leukemia derived cell line) of the present invention; Second, it is well known in the art of cell culture, to which the present invention relates, that the activity of a gene construct is not easily predictable from one cell line to another. Kutchera supports this premise, stating that "the expression of Cox-2 constructs varies depending on the cell used (see Fig. 4 and discussion)." Third, the Jurkat cell line used in the instant invention is not

disclosed in either Kutchera or Dannenberg nor do either disclose the activity of the Cox-2 promoter in other human T-cell leukemia cell lines to suggest that the present invention would have a reasonable expectation of success. Thus the instant claims are clearly not obvious over the cited references.

In order to capture this important element in the claims, Applicants have amended claim 9 to limit the cell of the invention to a Jurkat cell.

For the reasons set forth above, Applicants respectfully suggest that Claims 9-12 are not obvious over the cited references and the rejections under 35 U.S.C. § 103(a) should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims.

Applicants believe that no additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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